Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
I42327PC		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/001589	3	21.03.2003
International Patent Classification (IPC) or national classification and IPC		
Applicant		
IFAC GMBH & CO. KG		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 3 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/001589

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-20 as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* 1-15 received by this Authority on 01.08.2005 with letter of 01.08.2005

nos.* _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/001589

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-6, 8-9	YES
	Claims	7, 10-15	NO
Inventive step (IS)	Claims	1-6, 8-9	YES
	Claims	7, 10-15	NO
Industrial applicability (IA)	Claims	1-15	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Reference is made to the following documents:

D1: US 4 880 634 (P. SPEISER), 14 November 1989 (1989-11-14)
D2: US 5 188 837 (A.J. DOMB), 23 February 1993 (1993-02-23)

1. The application meets the requirements of **PCT Article 33(1)** because the subject matter of **independent claims 1, 8 and 9** is novel **(PCT Article 33(2))**.

Document **D1**, which is considered to be the prior art closest to the subject matter of **independent claims 1, 8 and 9**, discloses the following (the references in parentheses are to D1): a process for producing lipid nanopellets as an excipient system for pharmaceuticals (see **D1**, column 8, lines 18 to 56). Lipid nanopellets can be produced by melting a lipid mixture together with active substances and surfactants. A warm aqueous phase, which may contain emulsifiers, is added to the molten lipid mixture and is mixed in and dispersed **using a high-speed mixer**, and the mixture is then cooled. The high-speed mixer treatment is normally followed by **ultrasound treatment** to achieve the desired particle size. A suspension of active lipid

nanoparticles is obtained in which all the nanoparticles are uniformly penetrated by the emulsifiers.

The subject matter of **independent claims 1, 8 and 9** differs from what is known from **D1** in that the active mixture is an **iyotropic,** preferably gel-like **liquid crystalline mixed phase** produced **by gentle stirring without high-pressure homogenisation,** preferably by the shearing action of a domestic kitchen mixing appliance. The production process claimed in the present application also makes it possible to obtain **multiple dispersions.** The subject matter of **independent claims 1, 8 and 9** is therefore novel **(PCT Article 33(2)).**

The problem addressed by the present invention can thus be seen as that of providing an improved process for preparing dispersions or **multiple dispersions** of solid nanoparticle excipients using **iyotropic,** preferably gel-like **liquid crystalline mixed phases** produced **by gentle stirring without high-pressure homogenisation** or subsequent **ultrasound treatment.**

The solution proposed in **independent claims 1, 8 and 9** of the application involves an inventive step **(PCT Article 33(3))** because it is not obvious from the available prior art (document **D1**).

The subject matter of **independent claims 1, 8 and 9** therefore meets the PCT requirements in respect of novelty and inventive step.

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Claims 2 to 6 are dependent on **claim 1** and therefore also meet the PCT requirements in respect of novelty and inventive step.

2. The application fails to meet the requirements of **PCT Article 33(1)** because the subject matter of **independent claims 7, 10 and 11** is not novel over document **D1** **(PCT Article 33(2))**.

Document **D1** describes lipid nanopellets composed of a mixture of lipids and surfactants as an excipient system for pharmaceuticals. Lipid nanopellets can be produced by melting a lipid mixture together with active substances and surfactants. A warm aqueous phase, which may contain emulsifiers, is added to the molten lipid mixture and is mixed in and dispersed using a high-speed mixer, and the mixture is then cooled. A suspension of active lipid nanoparticles is obtained in which all the nanoparticles are uniformly penetrated by the emulsifiers. The lipids used are the same as those used in the present invention.

In the same way, the subject matter of **independent claims 7, 10 and 11** also lacks novelty over document **D2** **(PCT Article 33(2))**.

Document **D2** describes pharmaceutical excipients in the form of suspensions of solid lipid nanospheres. These are produced by melting a lipid mixture, which, together with a phospholipid, is mixed with a warm aqueous phase and dispersed, and is then cooled. The resulting spheres have a phospholipid coating not only

on the surface but also embedded in the surface. The lipids used are the same as those used in the present invention.

3. The application fails to meet the requirements of PCT Article 33(1) because the subject matter of **independent claims 7, 10 and 11** does not involve an inventive step **(PCT Article 33(3))**.

With regard to the subject matter of **independent claims 7, 10 and 11**, documents **D1 and D2** appear to be of particular relevance to the assessment of inventive step. D1 and D2 solve **the same problem**, namely that of providing dispersions of solid nanoparticle excipients whose make-up comprises a mixture of lipids, active substances and surfactants, and in which all the nanoparticles are uniformly penetrated by emulsifiers, using the same lipids as the present invention.

Thus, as far as novel subject matter is concerned, the present application does not appear to meet the requirements of **PCT Article 33(1)** and **33(3)** in relation to D1 and D2.